UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CAMDEN VICINAGE

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	MDL No. 2875 Honorable Robert B. Kugler, District Court Judge **Oral Argument Requested**

DEFENDANTS' REPLY IN SUPPORT OF MOTION TO PARTIALLY EXCLUDE OPINIONS OF DR. STEPHEN HECHT

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INTRODUCTION

Plaintiffs' opposition fails to rebut defendants' arguments that certain opinions offered by Dr. Hecht are inadmissible.

First, Dr. Hecht has no reliable basis to opine that defendants should have anticipated the formation of nitrosamines. Plaintiffs do not cite any cases holding that an expert can opine on the state of scientific knowledge without an objective basis for his or her opinions. And none of the scientific literature they cite comes close to providing the necessary support for such an opinion.

Second, Dr. Hecht should not be permitted to testify that defendants should have suspected that certain raw materials contained reactive impurities. The Federal Rules require an opinion to be disclosed in an expert report, not for the first time at a deposition. And in any event, plaintiffs have no evidence that ZHP's raw materials actually were contaminated, rendering this opinion irrelevant.

Third, and finally, Dr. Hecht should not be able to offer legal opinions, whether expressly or by parroting the language of regulatory standards.

ARGUMENT

I. DR. HECHT LACKS A SCIENTIFIC BASIS FOR HIS OPINION THAT DEFENDANTS SHOULD HAVE ANTICIPATED THE FORMATION OF NITROSAMINES.

As defendants explained in their opening brief, Dr. Hecht lacks any scientific basis to conclude that defendants should have anticipated that NDEA or NDMA

would be formed during the valsartan manufacturing process. Plaintiffs' arguments to the contrary are inconsistent with the relevant law and factual record.

First, plaintiffs argue that Dr. Hecht was not required to cite any scientific literature that warned of the risk of nitrosamine formation. Instead, they contend, he can simply assert that the complex reactions at issue were widely known and should have been expected, because "[o]pinions based solely on experience and knowledge are sufficient under *Daubert*." (Opp'n at 13 (citation omitted).) In so arguing, plaintiffs fail to address the scores of cases defendants cited in their opening brief holding that an expert who seeks to opine on the state of scientific knowledge must offer ***objective*** evidence, in the form of authoritative literature, surveys, or the like, rather than his or her own subjective opinions. (*See* Mem. at 12-13 & n.5; *see also* Reply in Supp. Mot. to Exclude R. Najafi ("Najafi Reply") at 2-4.)

Plaintiffs' own cases do not support their arguments either. *Westley v. Ecolab, Inc.*, No. 03-CV-1372, 2004 WL 1068805 (E.D. Pa. May 12, 2004) and *In re Front Loading Washing Machine Class Action Litigation*, No. 08-51, 2013 WL 3466821 (D.N.J. July 10, 2013) (both cited in Opp'n at 13), admitted expert testimony based on experience to demonstrate either common defect at class certification, *see Front Loading Washing Mach.*, 2013 WL 3466821, at *3, or causation, *see Westley*, 2004 WL 1068805, at *9; *see also Kannankeril v. Terminix Int'l, Inc.*, 128 F.3d 802, 809 (3d Cir. 1997) (causation opinion based in part on experience). They did not address

expert testimony about the state of scientific knowledge or what others should have known and expected. This distinction matters because while one's own personal experience can provide a basis to opine about physical processes, it cannot provide a basis to opine on what ***other people*** know or knew. *See, e.g.*, *In re 3M Combat Arms Earplug Prods. Liab. Litig.*, No. 19md2885, 2021 WL 684183, at *4 (N.D. Fla. Feb. 11, 2021) ("[m]ost courts have prohibited experts from testifying . . . about 'what doctors generally think,' unless the testimony is based on something more reliable than simply the expert's own experience as a doctor[]") (citation omitted).

Second, plaintiffs insist that objective scientific evidence does support Dr. Hecht's opinion that nitrosamine formation should have been foreseen. But none of the articles they cite supports that assertion. Contrary to plaintiffs' position, defendants do not contend that an article must "mirror[] the ***exact*** same conditions" used in valsartan manufacturing in order to be relevant. (Opp'n at 13 (emphasis added).) But an expert's opinion should be excluded if "there is simply too great an analytical gap between the data and the opinion proffered." *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997); *see, e.g.*, *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1248-49 (11th Cir. 2005) (reversing admission of testimony from expert who drew "unauthorized conclusions . . . the authors of the study [relied upon] d[id] not make"). That is the case here, with respect to both Dr. Hecht's opinions on NDEA formation and his opinions on NDMA formation.

TEA And NDEA Formation. Plaintiffs claim that the risk that TEA would react with sodium nitrate to form NDEA was "foreseeable based on the scientific literature" (Opp'n at 18), but nothing they cite supports that assertion.[1] Two of the studies address different amines producing different nitrosamines and do not even reference TEA at all. *See* Walter Fiddler et al., *Formation of N-Nitrosodimethylamine from Naturally Occurring Quaternary Ammonium Compounds & Tertiary Amines*, Nature 236, 307 (1972) (Opp'n Ex. 39) (ECF 2323-4); Zhi Sun et al., *Theoretical Investigation of N-Nitrosodimethylamine Formation from Nitrosation of Trimethylamine*, J. Phys. Chem. A, 114, 455-65 (2010) (Opp'n Ex. 40) (ECF 2323-4).[2] The third article likewise focuses on two different amines—not TEA.[3] And while the third article does mention in passing a single study related to TEA, the authors acknowledge that the study was immediately criticized. *See* Smith (1967). As explained in defendants' opening brief, the Smith (1967) article

[1] To the extent plaintiffs imply that Novartis was able to predict nitrosamine formation in the presence of sodium nitrite, that is contrary to the record. Novartis first mentioned sodium nitrite after the impurities had been identified. (*See* ZHP01390018 (cited in Opp'n at 9).)

[2] The Sun et al. (2010) article is also irrelevant because it merely proposed a theory regarding nitrosamine formation and did not offer any experimental support. (*See* Defs.' Opp'n to Mot. to Preclude Dr. Fengtian Xue, ECF No. 2322, at 7.)

[3] In addition to testing different amines, the authors of the article performed their test under significantly different conditions from those used in ZHP's TEA with quenching process. *See* Peter Smith & Richard Loeppky, *Nitrosative Cleavage of Tertiary Amines*, J. Am. Chem. Soc. 89, 1147-57 (1967) (ECF 2292-10).

actually supports defendants' position because it makes clear that the scientific community at large assumed that tertiary amines like TEA did not nitrosate. (*See* Mem. at 6.)

In addition to scientific literature, plaintiffs refence two internal ZHP documents. (*See* Opp'n at 18 (citing PRINSTON0076108); *id.* at 20 (citing PRINSTON00075927).) But both documents were written with the benefit of hindsight in 2018, after it had become clear that NDEA did form in valsartan. These documents say nothing about whether the process was foreseeable years earlier. (*See* Najafi Reply at 7.)

Zinc Chloride Process And NDMA Formation. Plaintiffs are similarly unable to identify literature or other objective evidence that Dr. Hecht used to support his opinion that ZHP should have expected DMF to degrade into DMA, and then form NDMA, during the Zinc Chloride process. As discussed in defendants' opening brief, Dr. Hecht relied overwhelmingly on a single sentence from *Purification of Laboratory Chemicals*, Armarego, WLF (4th Edition 1996; 6th Edition 2009) ("Armarego") that references DMF decomposition at its boiling point.[4] But as defendants explained—and as plaintiffs cannot refute—a single

[4] Another publication that plaintiffs cite suggests that even higher temperatures are required. *See* G. Long et al., *Concise Int'l Chem. Assessment Doc. 31: N,N-Dimethylforamide*, at 6 (WHO 2001) (cited in Opp'n at 15) (decomposition requires "[t]emperatures in excess of 350 ºC").

sentence in one publication (among thousands in the field) does not support Dr. Hecht's opinion that the possibility was so widely known in the scientific community that a reasonable pharmaceutical manufacturer should have foreseen it. (*See* Mem. at 16-17.)

In any event, Armarego does not support plaintiffs' position because it only mentioned decomposition at the boiling point, which is substantially higher than the temperature used in the Zinc Chloride process. Plaintiffs argue that the limitation is irrelevant because ZHP did not identify the textbook and "determine[] it [to be] inapplicable." (Opp'n at 16.) That argument misunderstands the nature of the *Daubert* inquiry. Dr. Hecht had the responsibility to identify reliable bases for his opinion that DMF degradation was foreseeable; it was not defendants' responsibility to demonstrate how they considered and discounted every conceivably relevant source of information. *See, e.g.*, *In re TMI Litig.*, 193 F.3d 613, 663 (3d Cir. 1999), *amended by* 199 F.3d 158 (3d Cir. 2000) (burden on proponent of expert). Plaintiffs also point to Dr. Hecht's testimony that if DMF can degrade at its boiling point, it could also degrade over a longer period of time at a lower temperature. (Opp'n at 19-20 (citing 1/13/23 Hecht Dep. 94:6-95:12 (ECF 2292-3)).) This is pure *ipse dixit* and therefore inadmissible. (*See* Mem. at 16; Najafi Reply at 4-5, 13.)

Beyond Armarego, plaintiffs point to "broader" literature that they contend supports the foreseeability of DMF degradation and NDMA formation. (Opp'n at

17-18.) But Dr. Hecht did not analyze any of the additional articles plaintiffs now cite or explain how they informed his opinion. The articles were simply listed, without analysis, in a supplemental reliance list provided two and a half months after his report was served and two days before his deposition. (*See generally* 10/31/22 Hecht Rep. (ECF 2292-8); Suppl. List of Materials Reviewed, Jan. 11, 2023 (Opp'n Ex. 29 (ECF 2323-4)).) That is not good enough. An expert must reliably explain how he used literature to inform his opinions, not simply list studies and wait for counsel to "fill in the gaps" in a brief. *In re Human Tissue Prods. Liab. Litig.*, 582 F. Supp. 2d 633, 667 (D.N.J. 2008). Moreover, the fact that Dr. Hecht did not find this literature in time for his report suggests that neither the articles, nor the potential degradation of DMF that they discuss, are well known in the chemistry community even today.

In any event, none of the late-disclosed publications suggests that defendants should have known DMF can degrade under conditions like those used in the Zinc Chloride process. The first, Jean Juillard, *Dimethylformamide: Purification, Tests for Purity & Physical Props.*, Int'l Union of Pure & Applied Chem. (Pergamon Press 1977) (cited in Opp'n at 17) notes the possibility of DMF degradation by heat or hydrolysis, but does not identify any particular conditions under which degradation can occur. The remaining two postdate the development of the Zinc Chloride process, and in one case, the product recall, and thus say nothing about the state of

knowledge at the time ZHP adopted the process. *See* Nakita Noel et al., *Unveiling the Influence of pH on the Crystallization of Hybrid Perovskites, Delivering Low Voltage Loss Photovoltaics*, Joule 1, 328-343 (2017); Jordan Kevin Magtaan et al., *Regeneration of Aged DMF for Use in Solid-Phase Peptide Synthesis*, J. Peptide Sci. 25 (2019) (both cited in Opp'n at 17-18).[5]

Finally, as was the case with his NDEA opinions (*see supra* at 4-5), plaintiffs seek to bolster Dr. Hecht's NDMA opinions by pointing to ZHP documents and claiming that DMA "was formed" in tests "matching the conditions in the [Zinc Chloride] process." (Opp'n at 20.) But this test, too, was done with the benefit of hindsight; as such, it does not shed light on whether the degradation of DMF into DMA was foreseeable. Plaintiffs also contend that a ZHP witness "admitted . . . that it was known in the chemistry community that DMF could decompose." (*Id.* at 17 (citing Dep. of Eric Gu 172:13-174:9, 183:12-21, Apr. 5, 2021 (ECF 2323-1, Ex. 34)).) What Mr. Gu actually said, however, was that decomposition was known to be possible "[u]nder certain circumstances" (for instance, at the boiling point), not that it was known to be possible under the conditions of the Zinc Chloride process.

[5] Plaintiffs contend that these articles cite earlier sources that likewise support Dr. Hecht's position. But Dr. Hecht never identified those earlier sources, even in his supplemental reliance list, strongly suggesting they were not well-known in the chemistry community.

For all of these reasons, plaintiffs' attempts to salvage Dr. Hecht's opinion that defendants should have foreseen nitrosamine formation should be rejected.

II. DR. HECHT SHOULD BE BARRED FROM TESTIFYING ABOUT THE POSSIBILITY OF CONTAMINATION IN RAW MATERIALS USED BY ZHP.

Plaintiffs also fail to refute defendants' argument that Dr. Hecht's opinion about potential contamination in raw materials: (1) was not properly disclosed in his expert report; and (2) does not fit the facts of the case.

First, Dr. Hecht failed to disclose his opinion about either DMA or DEA contamination in his report. That alone justifies exclusion. *See Krys v. Aaron*, 112 F. Supp. 3d 181, 207 (D.N.J. 2015) (cited in Mem. at 18);[6] *see also, e.g.*, *Forest Lab'ys, Inc. v. Ivax Pharms., Inc.*, 237 F.R.D. 106, 113 (D. Del. 2006) (expert should have been barred from testifying on topic that "was not included in his expert report" even though he "address[ed] the . . . issue during his deposition"); *Bedell v. Long Reef Condo. Homeowners Ass'n*, No. 2011-051, 2014 WL 1715441, at *6 (D.V.I. Apr. 30, 2014) ("Rule 26(a)(2) does not allow parties to cure deficient expert reports by supplementing them with later deposition testimony.") (citation omitted).

Plaintiffs contend that Dr. Hecht was entitled to offer new opinions at his deposition, but the only case they cite for that proposition, *nCube Corp. v.*

[6] Plaintiffs make no attempt to distinguish *Krys* or to explain why it should not be followed.

SeaChange Int'l, Inc., 809 F. Supp. 2d 337 (D. Del. 2011), does not support their argument. In *nCube*, the court admitted testimony from two challenged experts, mostly because the opinions at issue were adequately disclosed in the reports themselves or constituted "reasonable synthesis and/or elaboration of th[ose] opinions." *See id.* at 347-49 (citation omitted). Importantly, in so doing, the court reiterated the principle that "[t]estimony of expert witnesses is limited to the information contained in their expert reports." *Id.* at 347. Here, in contrast to *nCube*, Dr. Hecht's opinion that ZHP should have suspected that DMA and DEA were present in the raw materials they received from suppliers is not a logical extension of his opinions that DMA and DEA formed during valsartan production. Moreover, to the extent *nCube* can be read to suggest that significant "'elaboration' contained only in deposition testimony, and not in an expert report, is adequate to . . . comply with the disclosing party's obligations under Rule 26(a)(2)(B)," it is flatly inconsistent with the plain text of the Rule, which requires a "***complete*** statement of all opinions," Fed. R. Civ. P. 26(a)(2)(B) (emphasis added), in the report itself, as at least one other court has recognized, *see Asetek Danmark A/S v. CMI USA, Inc.*, No. 13-cv-00457, 2014 WL 6997670, at *1 n.1 (N.D. Cal. Dec. 9, 2014) (declining to follow *nCube* to the extent it allowed elaboration in a deposition).

Plaintiffs' alternative argument that Dr. Hecht sufficiently disclosed his opinion on raw-material contamination in his report is also meritless. Plaintiffs cite

two passages from the report that make passing reference to the possibility. (*See* Opp'n at 14 & n.6.) But defendants already acknowledged these passages, and plaintiffs ignore defendants' actual argument—i.e., that passing references unsupported by any scientific literature are insufficient to disclose an opinion. (*See* Mem. at 19-20; Najafi Reply at 2-3.)[7]

Finally, plaintiffs once again cite a handful of articles added to Dr. Hecht's supplemental reliance list on the eve of his deposition. As mentioned above, however, simply listing literature on a reliance list, especially late-disclosed literature, is legally insufficient to support an expert opinion. And in any event, none of the newly listed articles would support Dr. Hecht's opinion. Plaintiffs cite two publications for the idea that ZHP should have been on notice of potential DMA contamination in DMF, but those articles suggest that DMA is present in ***some*** DMF, not that it is a common impurity or that it was present in DMF that ZHP purchased. *See* Long et al. (2001) at 5; Juillard (1977) at 887 (both cited in Opp'n at 15). Indeed, one of the articles notes that DMA may be present in "impure solvent" but that "[g]ood quality DMF is commercially available." Juillard (1977) at 887. Plaintiffs'

[7] Plaintiffs also point to a sentence in a post-recall letter by ZHP employee Jun Du, cited by Dr. Hecht in his report, that refers to DMA as an "impurity/degradant of DMF." (10/31/22 Hecht Rep. at 3 (cited in Opp'n at 14).) Even assuming this passing mention of "impurity" suggests knowledge of the possibility of raw material contamination, as explained above, post-recall analysis is irrelevant to the question of foreseeability. (*See supra* at 4-5.)

supposed support for the idea that ZHP should have expected DEA contamination in TEA is even more tenuous. The article they cite simply states that TEA used in an experiment had been tested for DEA, not that such testing should be routine or that contamination should be expected. *See* Brian G. Gowenlock et al., *Nitrosative Dealkylation of Some Symmetrical Tertiary Amines*, J. Chem. Soc., Perkin Trans. 2, at 1110 (1979) (cited in Opp'n at 15).

Second, even if Dr. Hecht could reliably opine that ZHP should have known that raw materials could contain DMA or DEA impurities, that opinion would fail to fit the facts of the case because they offer no evidence that the materials ZHP used were, in fact, contaminated. Indeed, plaintiffs concede that a test of ZHP's DMF supply revealed no detectable DMA or DEA (*see* Opp'n at 16 n.9), and that Dr. Hecht did not perform any tests of his own in an attempt to refute those findings.

Nevertheless, plaintiffs speculate that such impurities could have been present at "amounts below the level of detection." (*Id.*) This does not suffice. As an initial matter, "[t]he subject of [a *Daubert*] motion is the proposed testimony of experts, not the theories of the lawyers." *In re Rezulin Prods. Liab. Litig.*, 369 F. Supp. 2d 398, 407 (S.D.N.Y. 2005). In addition, plaintiffs' theory of sub-trace contamination is entirely speculative, and therefore insufficient to carry their burden to demonstrate admissibility. *See, e.g.*, *Bowers v. NCAA*, 564 F. Supp. 2d 322, 350 (D.N.J. 2008) (*see also* Najafi Reply at 8-9). For essentially the same reasons, a passage in ZHP's

post-recall investigation that hypothesized that the presence of "DMA residue in [purchased] DMF could not be excluded" from the realm of possibility (*see* Opp'n at 15-16 (citing PRINSTON00075961)) would also fail to provide sufficient support—even if post-recall statements were relevant, which they are not. Finally, plaintiffs cite two purported Certificates of Analysis that they claim to have obtained—apparently by downloading them from the Internet in 2023 (*see* Dep. of Fengtian Xue, Ph.D. 144:13-22, Feb 3, 2023 (Opp'n Ex. 15) (ECF 2323-3))—and that mention trace DMA or DEA impurities in commercially-available DMF and TEA (*see* Opp'n at 16 (citing Opp'n Exs. 32 & 33)). While plaintiffs assert that these certifications come from products "sold by the same manufacturers who sold the DMF or TEA used by ZHP" (*id.*), they offer nothing to suggest they came from the particular products used by ZHP or that they were included with shipments that ZHP received during the relevant time periods.

In short, Dr. Hecht's opinion that ZHP should have been aware of the possibility that certain raw materials would contain reactive amine impurities was both untimely and unreliable. Accordingly, it should be excluded from trial.

III. DR. HECHT SHOULD BE PROHIBITED FROM OFFERING REGULATORY OPINIONS.

Finally, plaintiffs concede that Dr. Hecht is not qualified to offer "regulatory opinions . . . as to whether defendants' manufacturing practices or processes adhered to state and federal regulations." (Opp'n at 11.) Nor do they dispute that such

opinions would usurp the role of the Court in defining the applicable law and the role of the jury in applying that law to facts.[8] (*See* Mem. at 22-25.) Nonetheless, they propose admitting the substance of those opinions by allowing Dr. Hecht to testify as to whether ZHP performed "a sound scientific appraisal" and allowing the factfinder to "rel[y] on [that testimony] in determining whether the governing standards requiring 'a sound scientific appraisal' were met." (Opp'n at 11.)

While Dr. Hecht would be qualified to opine on the appropriateness of ZHP's risk evaluation as a general matter (if he could do so reliably), he is not qualified to offer opinions about what any law or regulation requires. Nor is it appropriate for Dr. Hecht to parrot the language of any regulatory standards in an obvious effort to admit legal opinions through the back door. *See Neumann v. Home Depot U.S.A., Inc.*, No. 20-00387, 2022 WL 3042914, at *7 (D. Ariz. Aug. 2, 2022) (prohibiting expert from using legal "terms of art" because they "impl[y] legal conclusions"). Allowing testimony to be framed in the language of legal standards would also cause unfair prejudice by suggesting to the jury that Dr. Hecht believes defendants broke the law.

[8] To the extent plaintiffs dispute this principle in their opposition to Defendants' Motion to Exclude the Opinion of Ramin Najafi, their arguments are without merit for the reasons explained in defendants' reply in support of that motion. (*See* Najafi Reply at 14-15.)

CONCLUSION

For the foregoing reasons, as well as those set forth in defendants' opening memorandum, Dr. Hecht's opinions should be partially excluded.

Dated: April 25, 2023

Respectfully submitted,

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on April 25, 2023, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system, which will send a notice of electronic filing to all CM/ECF participants in this matter.

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